

(19) World Intellectual Property Organization  
International Bureau



PCT

(43) International Publication Date  
9 September 2005 (09.09.2005)

(10) International Publication Number  
**WO 2005/082002 A3**

(51) International Patent Classification:  
C12N 5/02 (2006.01) C12N 5/08 (2006.01)  
C12N 5/06 (2006.01)

(21) International Application Number:  
PCT/US2005/005877

(22) International Filing Date:  
22 February 2005 (22.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
10/789,308 26 February 2004 (26.02.2004) US

(71) Applicant (for all designated States except US): THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK [US/US]; 412 Low Library, Mail Code 4308, 535 West 116th Street, New York, NY 10027 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): JESSELL, Thomas

[GB/US]; 461 Waldo Avenue, Bronx, NY 10471 (US). WICHTERLE, Hynek [CZ/US]; 4 Wahington Square Village, Apt. 15M, New York, NY 10012 (US). WILSON, Sara [GB/US]; 400 West 119th Street, Apt. 6F, New York, NY 10027 (US). LIEBERAM, Ivo [DE/US]; 435 Riverside Drive, Apt. 124, New York, NY 10025 (US).

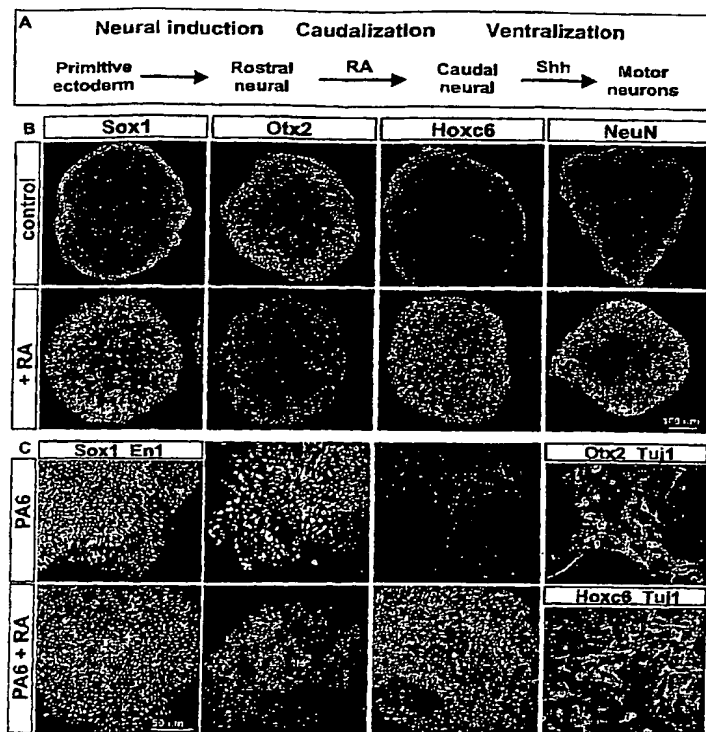
(74) Agents: SCHEINFELD, Robert, C. et al.; Baker Botts I.L.P, 30 Rockefeller Plaza, New York, N.Y. 10112-4498 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

[Continued on next page]

(54) Title: SYSTEMS AND METHODS FOR SCREENING FOR MODULATORS OF NEURAL DIFFERENTIATION



(57) Abstract: The present invention provides in vitro systems for use in identifying modulators of neural differentiation. Also provided are modulators identified by these systems. The present invention further provides methods for identifying a modulator of neural differentiation, a modulator of a Wnt signalling pathway, a modulator of Wnt-dependent neural differentiation, a modulator of a BMP signalling pathway, a modulator of BMP-dependent neural differentiation, a modulator of a Hh signalling pathway, and a modulator of Hh-dependent neural differentiation. Also provided are modulators identified by these methods.

Applicants: Thomas M. Jessell, et al.  
Serial Number: 10/789,308  
Filing Date: February 26, 2004  
Exhibit 60



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— with international search report

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

**(88) Date of publication of the international search report:**


16 August 2007

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/05877

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC: C12N 5/02( 2006.01),5/06( 2006.01),5/08( 2006.01)  USPC: 435/377,325,364,365 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/377,325,364,365  Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Medline		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CARPENTER, M.K. et al. Enrichment of neurons and neural precursors from human embryonic stem cells. Exp Neurol. December 2001 Vol. 172, No. 2, pages 383-397. Whole document, especially page 386, left column, first paragraph.	1, 3, 4, 10, 11, 14, 16,, 18-24, 26, 28, 30, 32-36, 38, 40-42
X	US 2002/0151056 A1 (SASAI et al.) 17 October 2002 (17.10.2002), [0023], claims 13,14, 56-59 [0105], [0176-0198]	1-9, 11, 14, 16-23, 28, 30-33, 36, 38, 40-42
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 11 June 2007 (11.06.2007)		Date of mailing of the international search report <b>26 JUN 2007</b>
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer  Daniel C. Garnett, PhD Telephone No. 571 272 1600

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US05/05877

### Continuation of Box II Reason 2:

Claim 13, 27, 29, 37, 39 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because the claim are not fully supported by the description. The application, as originally filed, did not describe: Any modulator identified by any of the claimed methods.

### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-12, 14, 16-26, 28, 30-36, 38 and 40-42, drawn to an in vitro system and methods for identifying a modulator of neural differentiation.

Group II, claim(s) 43-52, and claim 67, in part, drawn to methods for identifying a modulator of an FGF signaling pathway.

Group III, claim(s) 53-66, and claim 67, in part, drawn to methods for identifying a modulator of a retinoid signaling pathway.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I recites the special technical feature, neural differentiation, which is not required by the methods of Groups II or III.

Group II recites the special technical feature, modulator of an FGF signaling pathway, which is not required by the methods of Groups I or III.

Group III recites the special technical feature, modulator of a retinoid signaling pathway, which is not required by the methods of Groups I or II.